```
? s ant(w)1 or translocase(w)1
Processing
Processing
           22630  ANT
        13598295  1
              81  ANT(W)1
            5881  TRANSLOCASE
        13598295  1
              54  TRANSLOCASE(W)1
      S1     129  ANT(W)1 OR TRANSLOCASE(W)1
? s csa or cyclosporin
           27314  CSA
           46172  CYCLOSPORIN
      S2   63913  CSA OR CYCLOSPORIN
? s s1 amd s2
>>>Term "AMD" in invalid position
? s s1 and s2
             129  S1
           63913  S2
      S3       3  S1 AND S2
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S4       1  RD (unique items)
? t s4/3,k,ab/1

 4/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.

15279772   PMID: 15063741
  Adenine nucleotide translocase 3 (ANT3) overexpression induces apoptosis
in cultured cells.
  Zamora Monica; Granell Meritxell; Mampel Teresa; Vinas Octavi
  Departament de Bioquimica i Biologia Molecular, Facultat de Biologia,
Universitat de Barcelona, Diagonal 645, E-08028 Barcelona, Spain.
  FEBS letters (Netherlands) Apr 9 2004, 563 (1-3) p155-60, ISSN
0014-5793 Journal Code: 0155157
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Mitochondrial adenine nucleotide translocase 1 (ANT1), but not ANT2,
can dominantly induce apoptosis. Nothing is known, however, about the
apoptotic activity of ANT3. We have transfected HeLa cells with the three
human ANT isoforms to compare their potential as inducers of apoptosis.
Transient overexpression of ANT3 resulted, like ANT1, in apoptosis as shown
by an increase in the sub-G1 fraction, annexin V staining, low DeltaPsi(m),
and activation of caspases 9 and 3. Moreover, the apoptosis produced by
ANT3 was inhibited by bongkrekic acid and by cyclosporin A. The
pro-apoptotic activities of the ANT1 and ANT3 isoforms contrast with the
lack of apoptotic activity of ANT2. This finding may help to identify the
specific factors associated with the pro-apoptotic activities of ANT
isoforms.

  Mitochondrial adenine nucleotide translocase 1 (ANT1), but not ANT2,
can dominantly induce apoptosis. Nothing is known, however, about the
apoptotic...
```

... and 3. Moreover, the apoptosis produced by ANT3 was inhibited by bongkrekic acid and by **cyclosporin** A. The pro-apoptotic activities of the ANT1 and ANT3 isoforms contrast with the lack...
?

```
Set      Items   Description
S1         410   ANT(W)1 OR TRANSLOCASE(W)1 OR TRANSLOCASE1 OR ANT1
S2     3577661   INHIBIT? OR ANTAGONIST??
S3          66   S1 AND S2
S4          23   S3 AND PY<=1999
S5          12   RD (unique items)
? s bongkrekic
      S6     668  BONGKREKIC
? s s6 and s1
             668  S6
             410  S1
      S7       9  S6 AND S1
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S8       4  RD (unique items)
? t s8/3,k,ab/1-4

 8/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.

15279772   PMID: 15063741
  Adenine  nucleotide translocase 3 (ANT3) overexp
```

ocument Type: C
(A1) PRODUCTION OF ADENINE NUCLEOTIDE TRANSLOCATOR (ANT), NOVEL ANT LGANDS AND SCREENING ASSAYS THERRFOR; EXPRESSION VECTOR CODING TRANSPORT PROTEIN FOR USE IN THE DIAGNOSIS AND TREATMENT OF CELL PROLIFERATIVE, NERVOUS SYSTEM, DIABETIC AND VISION DEFECTS
(B2) PRODUCTION OF ADENINE NUCLEOTIDE TRANSLOCATOR (ANT), NOVEL ANT LIGANDS AND SCREENING ASSAYS THEREFOR
Inventors: Anderson Christen M (US); Clevenger William (US); Davis Robert E (US); Wiley Sandra Eileen (US)
Assignee: (A1) Unassigned Or Assigned To Individual
(B2) Migenix Corp
Assignee Code: (A1) 68000
Publication (No,Kind,Date), Applic (No,Date):
US 20020177185 A1 20021128 US 98185904 19981103
US 6906173 B2 20050614 US 98185904 19981103
Calculated Expiration: 20181103
Prior Publication(No,Date),Applic(No,Date):US 20020177185 A1 20021128
Continuation Pub(No),Applic(No,Date): (US 20020177185 A1) Compositions and methods are provided for producing adenine nucleotide translocator (ANT) polypeptides and fusion proteins, including the production and use of recombinant expression constructs having a regulated promoter. ANT ligands and compositions and methods for identifying ANT ligands, agents that bind ANT and agents that interact with ANT are also disclosed. (US 6906173 B2) Compositions and methods are provided for producing adenine nucleotide translocator (ANT) polypeptides and fusion proteins, including the production and use of recombinant expression constructs having a regulated promoter. ANT ligands and compositions and methods for identifying ANT ligands, agents that bind ANT and agents that interact with ANT are also disclosed.
Priority Applic(No,Date): US 98185904 19981103

Abstract: (US 20020177185 A1)
Compositions and methods are provided for producing adenine nucleotide translocator (ANT) polypeptides and fusion proteins, including the production and use of recombinant expression constructs having a regulated promoter. ANT ligands and compositions and methods for identifying ANT ligands, agents that bind ANT and agents that interact with ANT are also disclosed.

Abstract: (US 6906173 B2)
Compositions and methods are provided for producing adenine nucleotide translocator (ANT) polypeptides and fusion proteins, including the production and use of recombinant expression constructs having a regulated promoter. ANT ligands and compositions and methods for identifying ANT ligands, agents that bind ANT and agents that interact with ANT are also disclosed.

...Division Pub(No),Applic(No,Date): 5. The expression construct of claim 4 wherein the human adenine nucleotide translocator polypeptide is **ANT1** .; ...

...27. The expression construct of claim 26 wherein the human adenine nucleotide translocator polypeptide is **ANT1** .; ...

...The isolated polypeptide of claim 43 wherein the human adenine nucleotide translocator polypeptide is recombinant **ANT1** or a variant or fragment thereof...

...60. The method of claim 59 wherein the human adenine nucleotide

translocator polypeptide is **ANT1** .; ...

...at least one ANT inhibitor that is selected from the group consisting of atractyloside and **bongkrekic** acid...

...4. The isolated polypeptide of claim 1 wherein the host cell lacks an endogenous human **ANT1** adenine nucleotide translocator polypeptide as set forth in SEQ ID NO:31 and wherein the
?

Mitochondrial disease in mouse results in increased oxidative stress.

Esposito L A; Melov S; Panov A; Cottrell B A; Wallace D C

Center for Molecular Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Apr 27 **1999** , 96 (9) p4820-5, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: AG13154; AG; NIA; HL45572; HL; NHLBI; NS21328; NS; NINDS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

It has been hypothesized that a major factor in the progression of mitochondrial disease resulting from defects in oxidative phosphorylation (OXPHOS) is the stimulation of the mitochondrial production of reactive oxygen species (ROS) and the resulting damage to the mtDNA. To test this hypothesis, we examined the mitochondria from mice lacking the heart/muscle isoform of the adenine nucleotide translocator (**Ant1**), designated **Ant1** (tm2Mgr) (-/-) mice. The absence of **Ant1** blocks the exchange of ADP and ATP across the mitochondrial inner membrane, thus **inhibiting** OXPHOS. Consistent with **Ant1** expression, mitochondria isolated from skeletal muscle, heart, and brain of the **Ant1** -deficient mice produced markedly increased amounts of the ROS hydrogen peroxide, whereas liver mitochondria, which express a different Ant isoform, produced normally low levels of hydrogen peroxide. The increased production of ROS by the skeletal muscle and heart was associated with a dramatic increase in the ROS detoxification enzyme manganese superoxide dismutase (Sod2, also known as MnSod) in muscle tissue and muscle mitochondria, a modest increase in Sod2 in heart tissue, and no increase in heart mitochondria. The level of glutathione peroxidase-1 (Gpx1), a second ROS detoxifying enzyme, was increased moderately in the mitochondria of both tissues. Consistent with the lower antioxidant defenses in heart, the heart mtDNAs of the **Ant1** -deficient mice showed a striking increase in the accumulation of mtDNA rearrangements, whereas skeletal muscle, with higher antioxidant defenses, had fewer mtDNA rearrangements. Hence, **inhibition** of OXPHOS does increase mitochondrial ROS production, eliciting antioxidant defenses. If the antioxidant defenses are insufficient to detoxify the ROS, then an increased mtDNA mutation rate can result.

Apr 27 **1999** ,

... examined the mitochondria from mice lacking the heart/muscle isoform of the adenine nucleotide translocator (**Ant1**), designated **Ant1** (tm2Mgr) (-/-) mice. The absence of **Ant1** blocks the exchange of ADP and ATP across the mitochondrial inner membrane, thus **inhibiting** OXPHOS. Consistent with **Ant1** expression, mitochondria isolated from skeletal muscle, heart, and brain of the **Ant1** -deficient mice produced markedly increased amounts of the ROS hydrogen peroxide, whereas liver mitochondria, which...

... both tissues. Consistent with the lower antioxidant defenses in heart, the heart mtDNAs of the **Ant1** -deficient mice showed a striking increase in the accumulation of mtDNA rearrangements, whereas skeletal muscle, with higher antioxidant defenses, had fewer mtDNA rearrangements. Hence, **inhibition** of OXPHOS does increase mitochondrial ROS production, eliciting antioxidant defenses. If the antioxidant defenses are...

5/3,K,AB/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12693546 PMID: 10613907

Adenine nucleotide translocase - 1 , **a component of the permeability transition pore, can dominantly induce apoptosis.**

Bauer M K; Schubert A; Rocks O; Grimm S
Max-Planck-Institute for Biochemistry, 82152 Martinsried, Germany.

Journal of cell biology (UNITED STATES) Dec 27 **1999** , 147 (7) p1493-502, ISSN 0021-9525 Journal Code: 0375356
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Here, we describe the isolation of adenine nucleotide **translocase - 1** (**ANT - 1**) in a screen for dominant, apoptosis-inducing genes. **ANT - 1** is a component of the mitochondrial permeability transition complex, a protein aggregate connecting the inner with the outer mitochondrial membrane that has recently been implicated in apoptosis. **ANT - 1** expression led to all features of apoptosis, such as phenotypic alterations, collapse of the mitochondrial membrane potential, cytochrome c release, caspase activation, and DNA degradation. Both point mutations that impair **ANT - 1** in its known activity to transport ADP and ATP as well as the NH(2)-terminal half of the protein could still induce apoptosis. Interestingly, ANT-2, a highly homologous protein could not lead to cell death, demonstrating the specificity of the signal for apoptosis induction. In contrast to Bax, a proapoptotic Bcl-2 gene, **ANT - 1** was unable to

```
 s ant(w)1 or translocase(w)1 or translocase1 or ant1
Processing
Processing
           22630  ANT
        13598295  1
              81  ANT(W)1
            5881  TRANSLOCASE
        13598295  1
              54  TRANSLOCASE(W)1
               0  TRANSLOCASE1
             308  ANT1
      S1     410  ANT(W)1 OR TRANSLOCASE(W)1 OR TRANSLOCASE1 OR ANT1
? s inhibit? or antagonist??
Processing
         3224380  INHIBIT?
          892494  ANTAGONIST??
      S2 3577661  INHIBIT? OR ANTAGONIST??
? s s1 and s2
             410  S1
         3577661  S2
      S3      66  S1 AND S2
? s s3 and py<=1999
Processing
              66  S3
        37631515  PY<=1999
      S4      23  S3 AND PY<=1999
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S5      12  RD (unique items)
? t s5/3,k,ab/1-12
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